REMARKS

The Amendment

Claim 7 is amended to recite that the DNA sequences are directly deposited on the surface of the substrate. Support for the amendment can be found at page 11, lines 32-34.

Claims 34 and 35 are amended to delete the phrase regarding cross-contamination.

No new matter is added in any of the above amendments. The amendments are necessary in response to the Final Office Action. The Examiner is requested to enter the amendment and reconsider the application.

The Response

35 U.S.C. §112, First Paragraph Rejection

Claims 34, 35 and 39 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner states that the claims contain new matter in that there is no written basis for the generic phrase "essentially free of cross-contamination ...".

Applicants respectfully submit that the limitation "free of cross-contamination" is not a new matter because such feature is an inherent characteristic when a DNA solution is individually applied to each region of the microarray. However, to further prosecution, Applicants have deleted such phrase. In view of the claim amendments, the new matter rejection of Claims 34, 35 and 39 should be withdrawn.

35 U.S.C. §103(a) Rejection

Claims 7-40 are rejected under 35 U.S.C. §103(a) as being unpatentable over Pirrung, *et al.* (WO 90/15070). The rejection is traversed because Pirrung, *et al.*, do not teach or suggest a microarray of DNA sequences, which are at least about 50 subunits in length, individually applied to each region in the microarray and directly deposited on the surface of the substrate.

1. Non-enabling of the Reference.

Pirrung, *et al.* disclose a substrate having a plurality of polymer sequences in predefined regions (page 14, line 32). The reference primarily teaches a method of large-scale immobilized peptide synthesis. At page 14, line 30 through page 15, line 8, the reference describes:

> The invention is described herein primarily with regard to the preparation of molecules containing sequences of amino acids, but could readily be applied in the preparation of other polymers. Such polymers include, for example, both linear and cyclic polymers of nucleic acids, polysaccharides, phospholipids, and peptides having either α-, β-, or ω-amino acids, heteropolymers in which a known drug is covalently bound to any of the above, polyurethanes, polyesters, polycarbonates, polyureas, polyamides, polyethyleneimines, polyarylene sulfides, polysiloxanes, polyimides, polyacetates, or other polymers which will be apparent upon review of this disclosure.

The reference only speculates that nucleic acids, among many other polymers, can be immobilized on a substrate in predefined regions. There is no disclosure at all in the reference regarding a microarray having a density of 400 or more discrete regions of DNA sequences per cm^2 of substrate surface, wherein the DNA sequences contained in each discrete region are at least about 50 subunits in length and the DNA sequences are directly deposited on the surface of the substrate; therefore, the reference in no way enables one of ordinary skilled in the art to prepare such a microarray.

Applicants have amended Claim 7 to recite that the DNA sequences are directly deposited on the surface of the substrate. This limitation further distinguishes the substrate of the present invention from that having the DNA sequences associated with a substrate surface by hybridization or receptor recognition to a polymer immobilized on the substrate surface (see Office Action page 4).

2. DNA sequences of at least 50 subunits.

The instant microarray of DNA sequences having at least 50 bases has an additional advantage in that the microarray sequences can selectively hybridize with specific polynucleotides in a polynucleotide mixture. Microarray DNA sequences that have relatively short oligonucleotides (such as 8-10 bases) cannot selectively hybridize with a specific polynucleotide sequence in a mixture (see application at page 14, lines 7-16).

The Examiner argues that primers in the 8-10 base length range are known in the art for selective hybridization to specific polynucleotides in a mixture during amplification reactions; Applicants do not agree. It is well known that the specificity of hybridization depends on the length of the complementary DNA sequences. Although 8-10 base length primers are used in DNA amplification reactions, they are not highly specific or selective, thus resulting in impurities or by-products of the amplification reactions. However, amplification reactions are often followed by cloning, probing, or panning, which further selects the specific DNA sequences. On the contrary, the microarray of the present invention requires high specificity to achieve the specific detection of a particular gene in a complex mixture of a large number of genes. The instant microarray having DNA sequences of at least 50 bases provides high specificity for the desired purposes. -The instant application enables this and other unique aspects while the cited art fails to describe or even suggest such attributes.

3. Cross-Contamination.

Pirrung, *et al.* only teach synthesizing polymers (peptides) from monomers on the substrate; Pirrung, *et al.* do not teach or suggest individually applying DNA to each region in the microarray. Therefore, the inherent characteristics of the reference microarray substrate and the instant microarray substrate are different. The microarray of the present invention (Claims 7-40) is inherently free of cross-contamination because the DNA solution is individually applied to each region. Whereas the reference microarray is likely to be cross contaminated, as conceded in a much later filed U.S. Patent 5,744,305, which is a continuation-in-part application of the reference. For example, Column 17, line 59-67 of the '305 Patent describes:

> "Another important consideration is the fidelity of synthesis. Deletions are produced by incomplete photodeprotection or incomplete coupling. The coupling yield per cycle in these experiments is typically between 85% and 95%. Implementing the switch matrix by masking is imperfect because of light diffraction, internal reflection, and scattering. Consequently, stowaways (chemical units that should not be on board) arise by unintended illumination of regions that should be dark."

The Examiner argues that the reference shows and describes microarray preparation with the intended usage of sample binding assays wherein each region will result in a different binding

reaction result so that analysis of a multitude of different binding reactions may be performed in parallel. Applicants submit that the reference only describes the binding of a polypeptide sequence to a surface-bound peptide; the reference does not describe the binding of a DNA sequence to a surface-bound DNA.

For the reasons stated above, the 103(a) rejection of Claims 7-40 over Pirrung, *et al.*, should be withdrawn.

CONCLUSION

Applicants believe that the application is in good and proper condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 463-8181.

Respectfully submitted,

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